

FIG. 1

ASSOCIATION STUDIES (FIRST SCREENING)

NON ACITED	CONTROL S-76	VEE VIANCE	SOUTEARS 35.4.4	-3A<4
AFFECTED	CASES= 112	35 SPORADIC CASES	+77 FAMILIAL CASES	לייטרט ייטרט ייטרט
POPULATION	SAMPLE SIZE	POPULATION	CHARACTERISTICS	

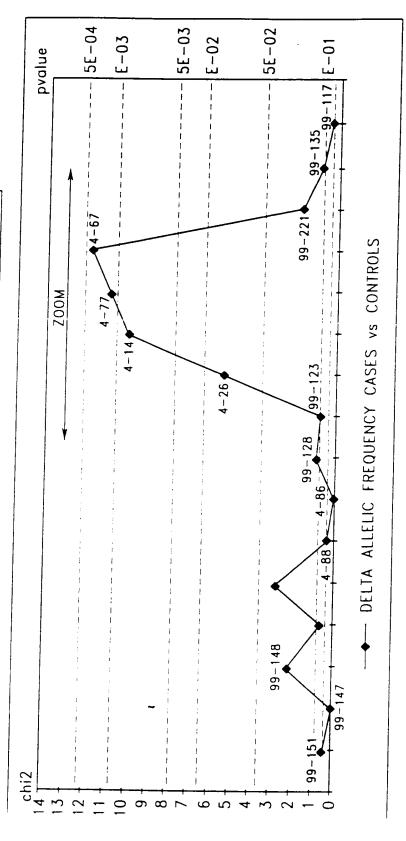


FIG.2

ASSOCIATION STUDIES (200M)

LINAFFER	CONTROLS	Y CE VE NE	203 TEAKS	PSA<4
AFFECTED	CASES (185)	47 SPORADIC CASES		130 LAMILIAL CASES
- , - }		CHARACTERISTICS	OF POPULATIONS	

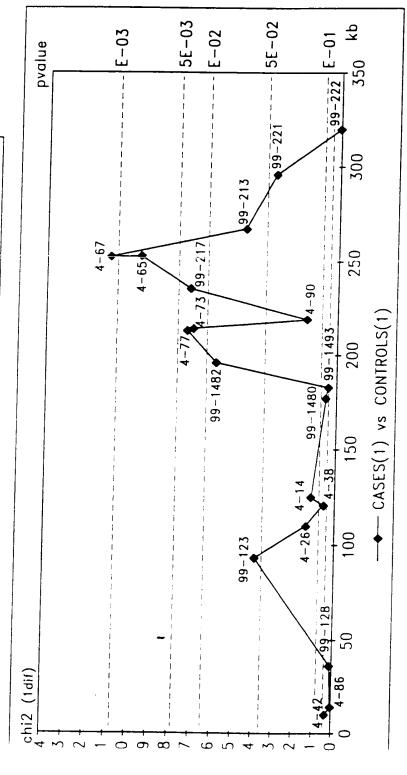


FIG.3

HAPLOTYPE FREQUENCY ANALYSIS

JLATIONS

INAFFFO	CONTROLS		^	PSA<4	
AFFECTED	CASES 2 (281)	143 SPORADIC CASES	1170 51411111 01050	TIJO LAMILIAL CASES	
		CHARACTERISTICS	OF POPILIATIONS	SI OLMINIS	

AARKERS 99-123 4-26 4-14 4-77 99-213 99-213 99-221 99-135 99-221 99-135 99-213 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221 99-135 99-221										_									_
99-123 4-26 4-14 4-77 99-217 4-67 99-213 99-221 99-135 PHPLOTYPE					PVALUE				9,00E-04 ***	6,00E-05 ***	1,00E-05****	9,00E-07****	2,005-05****	2,00E-05****	4,00E-05****	2,00E-04***	1,005-04***	3,00E-04***	6.00F-04***
99-123 4-26 4-14 4-77 99-217 4-67 99-213 99-22199-135 H0287809 B0189E0B					RELATIVE	RISK				1	6,78			!!				2,01	2.05
99-123 4-26 4-14 4-77 99-217 4-67 99-213 99-22199-135 H0287809 B0189E0B			PLOTYPE	QUENCIES		CONTROLS	(3)		5 0,018	5 0,016		7 0,013	7 0,025	7 0,027	2 0,109	0,134	5 0,112	5 0,146	5 0,129
99-123 4-26 4-14 H0287809 80189508 2,00E-01 1,00E-01 1,00E-01 C A C A C A C A C A C C A C C A C		.07		¥.		CASF	(2)		0,07	60'0	0,116	0,1	0 -	0,1	0,22	0,25	0,22(0,256	0,23
	99-123 1-26	H0287809 B0189£08	11453	GENES	2.00F-011 00F-01	1	<18KB> <15KB> <8RKR> <72KB> <17KB> <15KB>	VBX001< <arx67> <arcin co<="" court="" cruit="" td=""><td>V S V V V V V V V V V V V V V V V V V V</td><td>V 9</td><td>0TYPE 5<171KB> 6 A</td><td>¥ 9</td><td>A 5</td><td>A 0 1</td><td></td><td></td><td></td><td></td><td>5)</td></arcin></arx67>	V S V V V V V V V V V V V V V V V V V V	V 9	0TYPE 5<171KB> 6 A	¥ 9	A 5	A 0 1					5)

FIG.4

HAPLOTYPE SIMULATIONS (100 ITERATIONS)

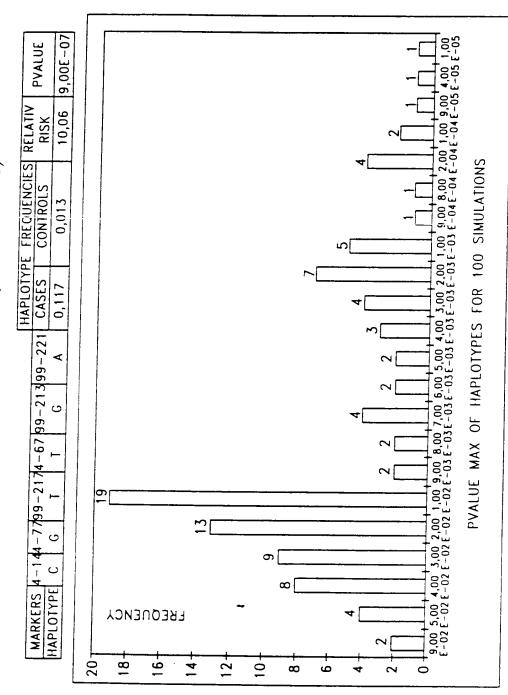


FIG.5A

HAPLOTYPE SIMULATIONS (100 ITERATIONS)

	PVALUE	2000	3,00t -0/
RFI ATIV	RISK	10.06	00'0
PE FREQUENCIFS	CONTROLS	0.013	0.00
HAPLOTY	CASES	0.117	
	1399-221	∢	
	-67 99-213	1 6	
•	799-2174-0	—	
	4-144-7	9)	
	MAKKERS	HAPLOTYPE	

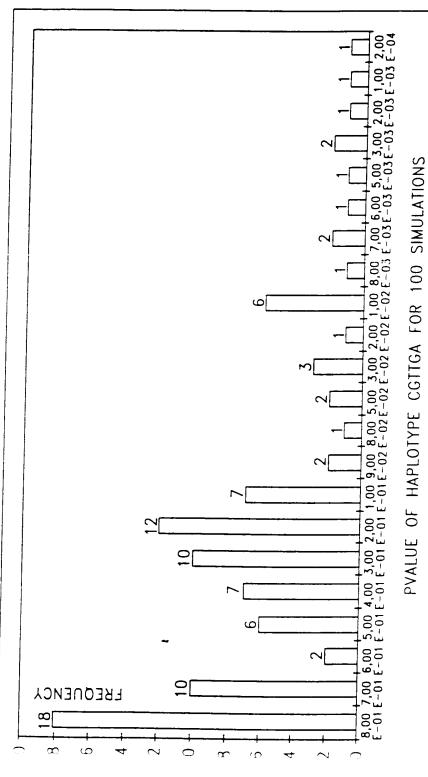


FIG.5B

	00010 00000	MICKUSEU. OLIGOS POSITIONS•	1-23125-47 (COUPLEUFUTABY	1-23 25-47 (COMPLEMENTARY	~	1-23 25-47 COMPLEMENTARY	~	25-47	1-23 25-47 (COMPLEMENTARY	11-23 25-47 (COMPLEMENTARY	_
	DACE	DASE	2	A/G	()	၁/၁ ၁/၁	\ <u>`</u>	C/1	<u></u>) \ \	و ۷
	SEQ ID POLYMORPHISM	POSITION.	24	24	24	24	24	24	77	74	74
	SEQ ID	ż	6	4 C	25		25	S.	0 n	0	000
	RP SEQUENCE	*****	TOACCACTOCTACCACTOC	CACTCTATCCTTTCATCCTC	GGAAACCTACTCATTCATAG	CITIATITION	16AAA6A6111A111A116166		TCATTCGTCTACCTO	AACACTCCCATTCTCC	201011000000000000000000000000000000000
5	 		S C	7	42	7 7	77	45	46	•	
	PU SEQUENCE	AAAGCCACCACTACAACC	TACAGCCCTGTAAGACAC	TCTAACCTCTCATCCAAC	TGITGATTTACAGGCGGC	GGIGGGAATITACTATAT	AAGTICACCTICTCAAGC	ATACTGGCAGCGIGTGCTTC	CCCTTTTCTTCACTGTTC	16GAAGTIGTTATTGCCC	
SECTO	N.(MUT)	30	31	32	£. €.	34	35	36	37	38	
O DYCAN SEO ID	MARNER	99-123 21	19 4-26 22	189 4-14 23	465 4-77 24	99-217 25	463 4-67 26	27 28 - 213 27	87 177-66 6	67 66 68	

FIG.6A

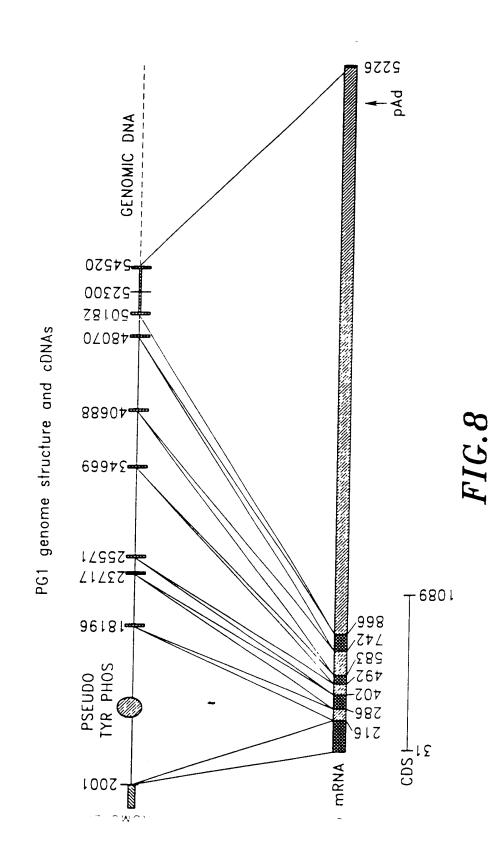
SITIONS ARE GIVEN RELATIVE TO THE SEQUENCE OF THE CORRESPONDING MARKER (1.8. SEQ ID Nº 21-38 AND 57-62)

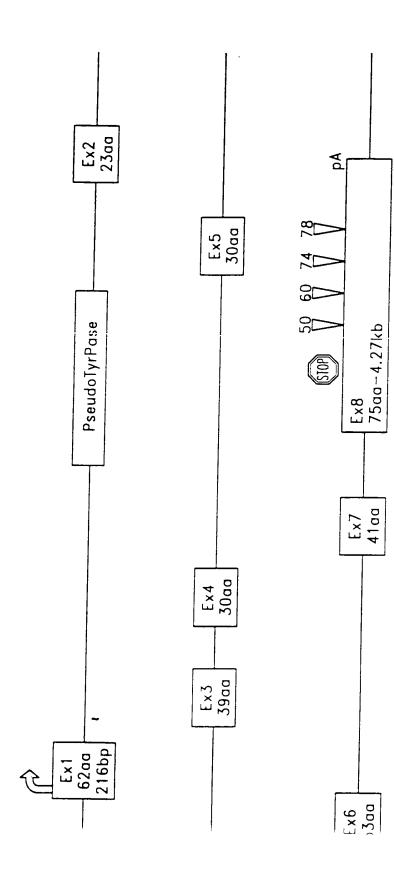
	SEQ ID POLYMORPHISM AASE MICBOSED OLICE SCIENCE	MICHOSER. OLIGOS POSITIONS.	1-23 25-47 (COMPLEMENTARY)	G/C 1-23 25-47 COMPLEMENTARY	1-21/25-17 /COURTENENT OF
	PASE	2	V ∨ C	၁ <u>/</u> ၁	
	POLYMORPHISM	PUSITION.	24	24	24
	SEQ ID	z	99	۵/	200
	RP SEQUENCE		CICITOCITA A CACCOTO	TGGCTCTGCATTTCTTCC	221121122222222
	SEO ID	2.3	6 6	5 45	}
	PU SEQUENCE	ATCAAATCAGTGAAGTCTAAC	ATCGCTGGAACATTCTGG	GATTTAAGCTACGCTATTAG	
0.000	N'(MUT)	09	61	62	
01 013	MARKER 35 N	6399-1482 57	4-73 58	4-65 59	1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -
	ا ر	7	<u>ئ</u>	· ·	1

FIG.6B

SITIONS ARE GIVEN RELATIVE TO THE SEQUENCE OF THE CORRESPONDING MARKER (1.e. SEQ ID Nº 21-38 AND 57-62)

EXON Phase	START	END	5' SPsite	PHASE	3' SPsite
Ex1 +0	2001	2216			GTGAGC
Ex2 +1	18196	18265	TAG	+0	GTTTGTA
Ex3 +0	23717	23832	CAG	+2	GTAACT
Ex4 +0	25571	25660	CAG	+0	GTAAGA
Ex5 +2	34669	34759	CAG	÷0	GTAAGT
Ex6 +1	40688	40846	TAG	+1	GTAAGT
Ex7 +2	48070	48193	TAG	+2	GTGAGT
Ex8	50182	54523	TAG	+1	
ATG codon	2031	2033			
STOP codon	50405	50407			
POLY Ad site	54445	54450			



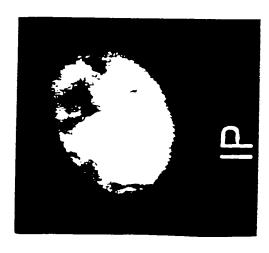


		box 1	box 2	box 3
PG1	Hs	NHQ 81-83	FPEGTR 160-165	LDAIYDVTV 211-219
AF003136 (Genbank)		NHQ 630-632	FPEGTR 712-717	LDAIYDVTV 762-770
Z72511 (Genbank)	Се	48 NHR 50	FPEGTD 129-134	VEYIYDITI 204-212
P38226 (Swisspor	Sc t)	111 NHQ 113	FPEGTN 223-228	IESLYDITI 271-279
P33333 (Swisspor	Sc t)	81 NHQ 83	FPEGTR 154-159	-
Z49770 (Genbank)	Sc	116 NHQ 118	FPEGTN 215-220	LDAIYDVTI 265-273
P26647 (Swissport	Ec t)	72 NHQ 74	FPEGTR 145-150	-
Z49860 (Genbank)	Bn	-	FVEGTR 90-95	VPAIYDMTV 138-146
U89336 (Genbank)	Hs	95 NHQ 97	FPEGTR 168-173	-
U56417 (Genbank)	Hs	103 NHQ 105	FPEGTR 176-181	-
AB005623 (Genbank)	Mm	100 NHQ 102	FPEGTR 173-178	
Z29518 (Genbank)	Zm	91 NHR 93	FVEGTR 170-175	VPAIYDTTV 218-226

Hs = Homo sapiens, Ce = Caenorabibitis elegans, Ec = Escherichia coli; Sc = Saccharomyces cerevisiae, Bn = Brassica napus, Zm = Zea maize, Mm = Mus Musculus

Note: Funcitional acyl glycerol transferases all contain boxes 1 and 2 and not box 3. Proteins most related to PG1 contain the 3 boxes with a high degree of conservation.

^{- =} pattern absent from protein sequence



GFP

PC3 PG1



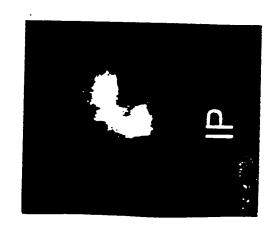


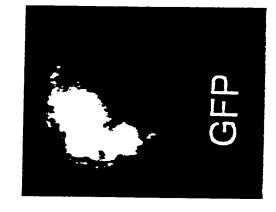






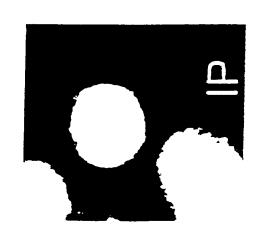
FIG. 10





PC3 PG1 1-4







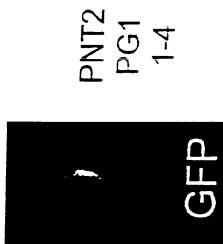
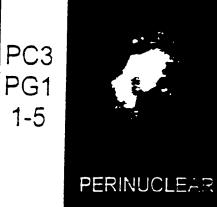
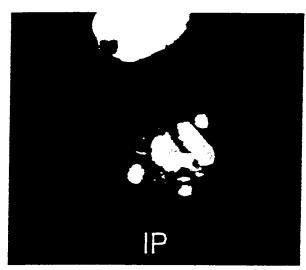


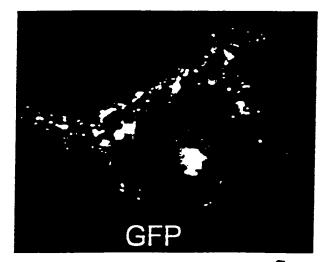


FIG. 11









PNT2 PG1 1-5

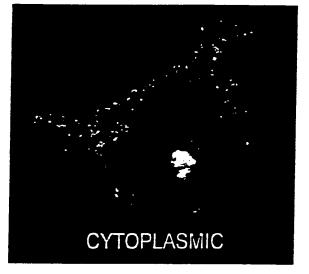
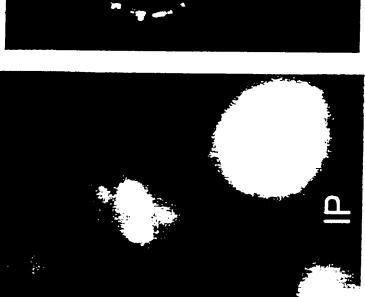
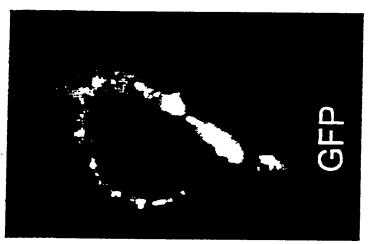
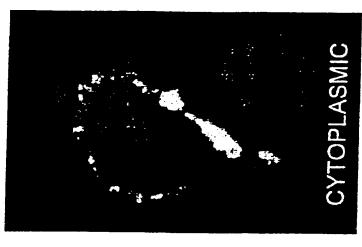


FIG. *2







PNT2 PG1 mut229

FIG. 13

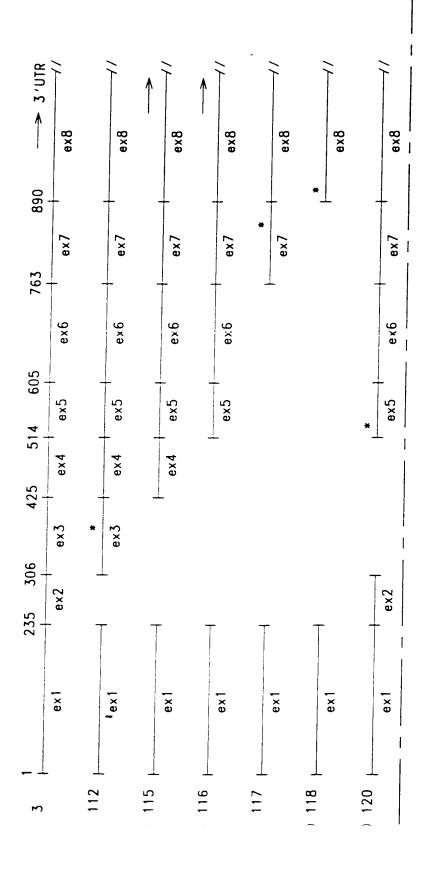
FIG. 14

FIG. 14A

FIG. 14B

Alternative splicing

-1G. 14A



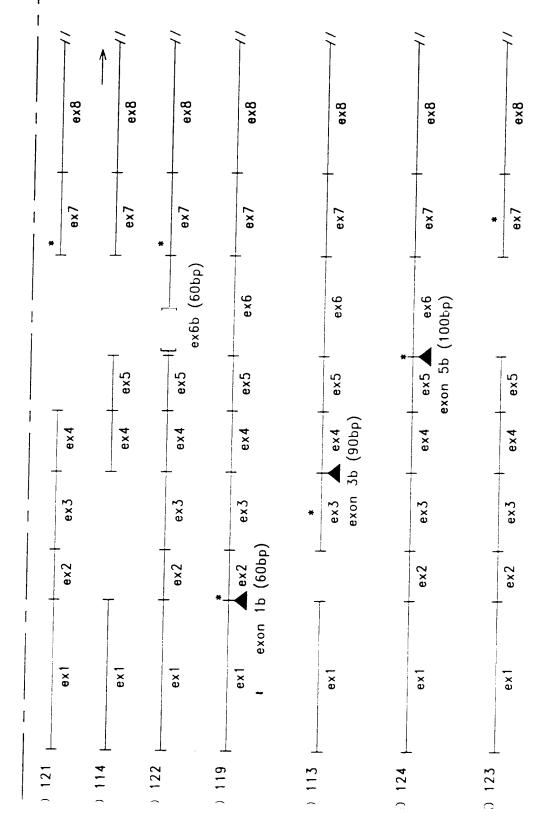


FIG. 14B

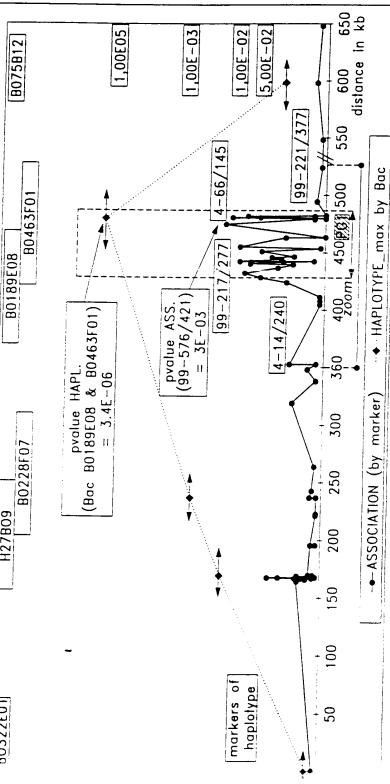
	$oldsymbol{\omega}_{oldsymbol{\omega}} = oldsymbol{\omega}_{oldsymbol{\omega}} oldsymbol{\omega}_{oldsymbol{\omega}} oldsymbol{\omega}_{oldsymbol{\omega}}$
. ec	
Printer	CP22 CP22 CP22 CP22 CP22 CP22 CP22 CP22
Pr	
PG1exon13	+++++++++++++++++++++++++++++++++++++++
PG1exon14	+++++++++++++++++++++++++++++++++++++++
PG1exon15	+
PG1exon16	- + - + + NT'- ++ + +
PG1exon:7	# : # : # : # : # : # : # : # : # : # :
PG1exon18	++++++++++++++++++++++++++++++++++++++
PG1exon24	
PG1exon25	+ + - + +
PG1exon26	
PG1exon27	<u> </u>
PG1exon28	+NT'
PG1exon35	- + + + + + + + NT; + + + + + + + + + + + +
PG1exon36	
PG1exon37	
PG1exon38	
PG1exon46	
PG1exon47	
PG1exon48	
PG1exon57	· · · · · · · · · · · · · · · · · · ·
PG1exon58	
PG1exon68	
PG1exon115	- サーナ・ナーナ・ナ・ナ・ナ・ト・ナー・ナ・ニ・ナーナ・ナ・ナ・ナ・ナー ニ・キュニ・ニ・キュー・キュー・キュー・
PG1exon1b2	<u> </u>
PG1exon1b3	
PG1exon1b4	
PG1exon155	+ + + + + NT'+ +
PG1exon156	
PG1exon157	+'+-+
PG1exon153	+ - + - NT - + - +
PG1exon3b4	++++++++++++++++++++++++++++++++++++++
PG1exon3b5	NT:
PG1exon3b6	
PG1exon3b7	+++
PG1exon3b8	+ + + NT - + - + + +
PG1exon5b6 PG1exon5b7	+!-!+ + +: NT[+:-:-:
PG1exon5b8	
PG1exon56b	<u> </u>
PG1exon46b	
PG1exon36b	
PG1exon26b	++++++++++++++++++++++++++++++++++++++
PG1exon16b	++++++++++++++++++++++++++++++++++++++
<u> </u>	

 $\widehat{f+1}$ alternative solicina form with combination of exons 13478 instead of 1345678

1113. 16

ASSOCIATION STUDIES HAPLOTYPE FREQUENCY ANALYSIS (chrom 8p23)

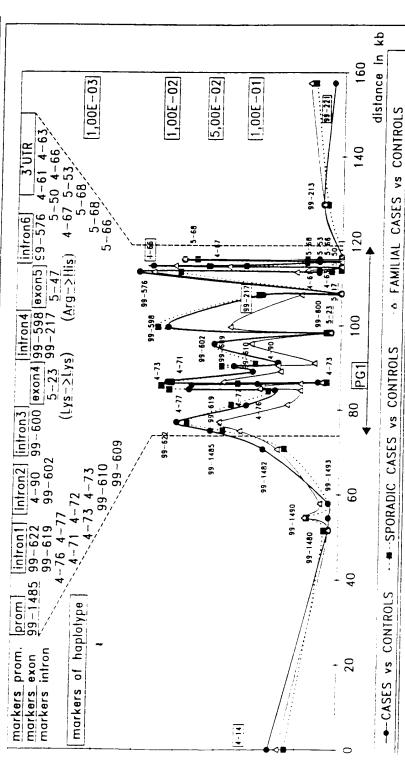
			2	
UNAFFECTED N=[130;313]	CONTROLS	<28 unaffected (65 years or older) & <289 controls (65 years or older with PSA<4)	B0189E08 B0463F01	pvalue HAPL. 80189E08 & B0463F01) = 3.4E-06
 AFFECTED N= [275;491]	ALL CASES	[275,491] all cases	H27B09 B0228F07	(Bac B0189EC
POPULATIONS		characteristics of populations	B <u>0322E01</u>]	-



F11 1

ASSOCIATION STUDIES PG1 (8p23)

UNAFFECTED N-[120.212]	0.001]	CONTROLS	<28		(65 years or older with PSA<4)
	FAMILIAL CASES		1-107 famili-1	v-197 Idmilial cases	
AFFECTED N= [275;491]	SPORADIC CASES		<=294 snorndice cases	מפרום בסופים	
	ALL CASES		<=491 all cases		
ATIONS		- deligination	ulations		

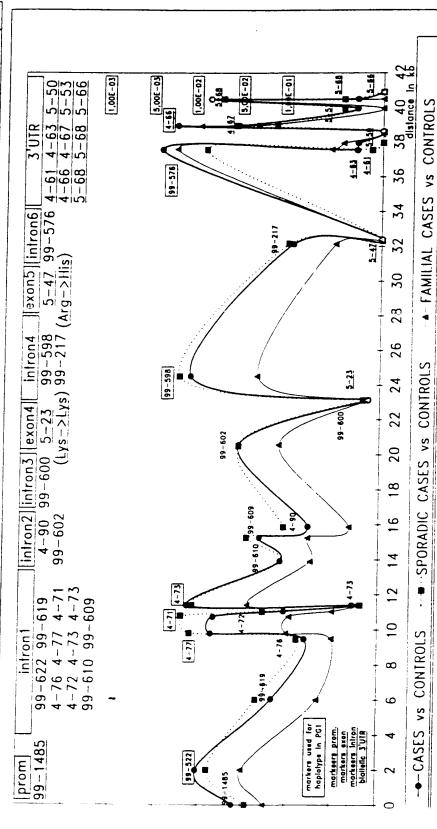


ASSOCIATION STUDIES

FIL: 18A

PG1 (8p23)

UNAFFECTED N=[130:313]	COCTACO	CONTROLS	<28 ur		(65 years or older with PSA<4)	
	FAMILIAL CASES			<=19/ tamilial cases		
AFFECTED N= [275;491]	SPORADIC CASES		- 201 canada	1 234 sportatics cases <=19/ tamilial cases		
	ALL CASES		2491 JU 1015	20202		
ATIONS				Sugions		



0		_		Ī	1	T	Ī	Ī	Ī	Τ	T-	Ī	Ì	\top	T	T	ī	Ĭ	ī	T
Attributable	4514	17.58	QN	GN	13.15	18.16	18.64	13.25	26.76	QN.	Q	9.32	QN	QN	Q	8.46	18.40	QN	13.16	10.97
Frea(randoms)	(ee.).	0.29	\$QN	S	0.41	0.31	0.28	0.31	0.52	QN	QN	0.28	QN N	QN	ON	0.28	0.24	QN	0.24	0.24
Pvalue		2.53E-02	9.64E-03	6.93E-02	1.57E-01	1.35E-02	1.43E-02	9.43E-02		8.33E-02	4.83E-02	1.68E-01	2.69E-02	7.52E-01	7.29E-03	1.07E-01	3.18E-03	0,527 §	4.68E-03	2.39E-02
Odd Ratio		.44	1.51	1.37	1.23	1.43	1.49	1.29	1.48	1.30	1.36	1.25	1.44	1.01	1.55	1.20	1.72	1.76	1.43	1.33
abs diff % (fq(cases)— (fq(controls))	7.7	*·/	10.	D.8	ر.	7.4	8.5	5.7	7.6	b.2	,	4.4	7.4	5.0	3.6	0.0	7.6	0.5	7.0	4.9
Freq(controls)	0.24	27.0	0.42	77.0	0.08	07.0	07.0	0.30	72.0	0.37	0.30	0.23	67.0	0.34	0.20	0.20	7.0	0.00	00	0.20
Freq(cas)	0.32	0.52	0.28	112	24.0	7.0	10.0	بماز	0.32	-	ءاز		200	35	0.33	0.27	0.01	0.0	25.0	
Polym.	1/*9	1/9	1/3	~ ~	2/5	√ `	~ `	2/5	ィー	1 2/ V	~ `	_ `	- 7/1 - 1/A	G/A	~	, · · ·	Z/V	٦ <u>`</u>	√	2.0
PG1	prom	in 1	in	2	2	in in	2	1	1		in?	in2	in3	in 4	in4	ju6		3'UTR	3'UTR	
⊕ of Aers	39 : 5 /251	39 6 /9 5	39 61 41 41	4 6 2	4 / 1	4 13	4 2 27	4 1 14	99 61 /250	6 4/2	4 10 83	E. 755	99 F 492	$3 \cdot 4/1\overline{3}$	77	99 /421	4 . 1 . 69	4 · 6 · 45	4	

§ Test Fisher—\$ ND: Not done —* disease associated allele / not associated allele

FIG. 18B

FIG. 19A

HAPLOTYPE FREQUENCY ANALYSIS

POPULATIONS	AFFECTED	UNAFFECTED
sample sizes	CASES (n=491)	CONTROLS (n=317)
characteristics of populations	294 sporadic cases + 197 familial cases	28 unaffected (65 years or older) + 289 controls (65 years or older with PSA<4)

			4-14/240	99-217/277	1-66/145	99-221/377
DC1 (-27	1	7 14/240			33-221/3//
PG1 (8	3p23	·)		in4	3'UTR	
distance bet	ween	mks	<10	0kb> <17	kb> <43	kb>
size (cases v	s cor	ntrois)	481 vs 305	481 vs 302	481 vs 300	481 vs 303
frequency % (co	ises/	controls)	65,7/62,1(C)	31,3/27,5(C)	25,1/19(C)	42,7/42,91 (A)
abs diff freq. all.	(case:	s-controls)	3.6	3.8	6.2	0
pvai	1e		1.47E-01	1.07E-01	4.68E-03	7.52E-01
Hardy Weindeberg		cases	5.84E-01	6.55E-01	2.54E-01	5.84E-01
Disequilibrium		controls	4.80E-01	2.21E-01	3.71E-01	2.54E-01
HAP 1 <43kb>		451 vs 297			% C (11)	A :
HAP 2 <17kb>		451 vs 296		T	C.	
HAP 3 <117kb>		452 vs 299	C			
HAP 4 <100kb>		479 vs 302	C	T		Í
HAP 5 <60kb>		476 vs 300		T	显然象	K.
HAP 6 <160kb>	PT2	476 vs 303	C			c
HAP 7 <160kb>		447 vs 297	C		C/	X.
HAP 8 <60kb>		446 vs 294		T	C	A
HAP 9 <117kb>		450 vs 296	C	T	C	
HAP 10 <160kb>	PT3	474 vs 300	С	T		A
HAP 11 <160k5>	PT4	445 vs 294	C	Ţ	C	A

	otype encies				
cases	controls	Odd ratio	Chi-S	Pval	ue
0.116	0.067	1.83	9.85	(1.7e-03)	***
0.243	0.183	1.43	7.49	(6.2e-03)	**
0.182	0.130	17.49	7.18	(7.3e-03)	**
0.217	0.188	1.20	1.88	(1.7e-01)	*
0.155	0.132	1.20	1.54	(2.1e-01)	*
0.373	0.346	1.12	1.16	(2.7e-01)	*
0.095	0.042	2.39	14.62	(1.3e-04)	****
0 117	0.065	1.93	11.33	(7.3e-04)	***

	9			*1	•
0.095	0.032	3.18	21.59	(3,4e-06)	****

1G. 19B

HAPLOTYPE FREQUENCY ANALYSIS PG1 (8p23)

markers	4-14/240	4-14/240 99-217/277	4-66/145	4-66/145 99-221/377
of haplotype Max		in4	3'UTR	•
	၁		ن	V
Total Control			,	C
distance Derween mks		<100kb> <17	<17kb> <	<43kb>

œ.			*****	*****	****	****	****			**	*****	****	*	*****
eulov 9			\$ 40F-06	+	+	+	+	3.50E 04	J. 305 - 04	9.40E-02	1.80E-05	2.20E-05	1.00E-02	+
chi-S			21.59	20.91	12.13	19.73	12.04	12.75	6.70	7.70	18.33	17.98	6.59	21.33
ppo	ratio		3.18	3.56	2.60	3.23	3.20	2.82	20.0	2.00	5.32	3.83	2.48	4.26
haplotype	frequencies	controls	0.032	0.032	0.032	0.032	0.032	0.032	0.000	0.032	0.032	0.032	0.032	0.032
oldah	fredu	CGS8S	0.095	0.105	0.079	0.096	0.095	0.085	0.062	2000	0.030	0.112	0.075	0.123
sample sizes		cases vs control	455 vs 294	171 vs 294	271 vs 294	266 vs 294	85 vs 294	178 vs 294	67 vs 294	179 45 201	#67 CA CA	۲ ۲	93 vs 294	79 vs 294
		PG1	s control	(<=65 years) vs controls	(>65 years) vs control	cases vs controls	dic cases (<=65 years) vs controls	idic cases (>65 years) vs controls	mative sporadic cases vs controls	cases vs controls		Signification (single form) (single form)	di cases (>ba years) vs controls	dal cases (>=3 caP) vs controls

F/G. 20

HAPLOTYPE FREQUENCY ANALYSIS (PG1)

			99-622/95	4-77/151	4-71/233	4-73/134	99-598/130	99-576/421	4-66/145	han	hanlotune				
Marke	Markers in PG1	4-	G/T	C/G	A/G	5/2	A ∕G	9/2	153						
				Inf	=		In4	ln6	3.UTR	- Lucius	fractional				
Size (Cas	size (cases vs controls)		336 vs 108	363 vs 173	336 vs 130	352 vs 129	347 vs 126	355 vs 129	456 vs 306		2011010				
c frequenc	frequency % (cases / controls)	ntrols)	52/42 (G)	34/26 (G)	34/26 (A)	52/42 (G)	35/25 (G)	27/17 (G)	25/19 (C)						
silelic frequ	sitelic frequency % (randoms)	18)	QN	31 (G)	28 (A)	52 (G)	Q	24 (G)	24 (C)						
if freq all.	if freq all. % (cases controls)	rots)	101	7.4	8.3	9.7	9.2	9.2	6.2	CB868	cases controls	9	Attabase		
			9.64E 03	1 35E-02	1 43E-02	7 29E 03	7 29E 03	3 18E-03	4 68E 03			Raffo		Ad	Pvalue
ovalue (ca	ovalue (cases vs controls)		:	:	:	:	:	:	:					(ceses vs controls)	ontrols)
ŏ	Odd Ratio		151	1 43	1 49	1 48	1.55	1.72	1 43						
Attribu	Attributable Risk %		QN	18 16	18 64	26 76	QN.	8 46	13 16						
ardy	C.8569		7 52E-01	7.52E-01	5.84E-01	7 52E-01	7.52E-01	7.52E-01	3 43F-01						
ullbrium	controls	8	4 39E 01	4 03E-01	1.21E-01	7 52E 01	6 52E 02	7 52E 01	1.29F.01						
type 1	2 MKS 33	339 vs 167								1920	0.163	9			
Type 2	3 MKS 33	330 vs 122		٠						0 259	0 147	202	60.61	(6.70.05)	
ype 3	4 MFS 31	312 vs 122								0 259	0.147	2 02	2	(4 to 04)	
lype 4		311 25 121	`			8				0.26	0 148	201	Q¥	(4 8e 04)	
El :	6 MM S	309 vs 121		8		Q		X		0 258	0 149	2	OH.	(5 30 04)	
2 216	\dashv	230 45 23		La Suille	within	1.	7778777	1.5	6.77	0 255	0 146	2	CN	(1 6e 03)	:

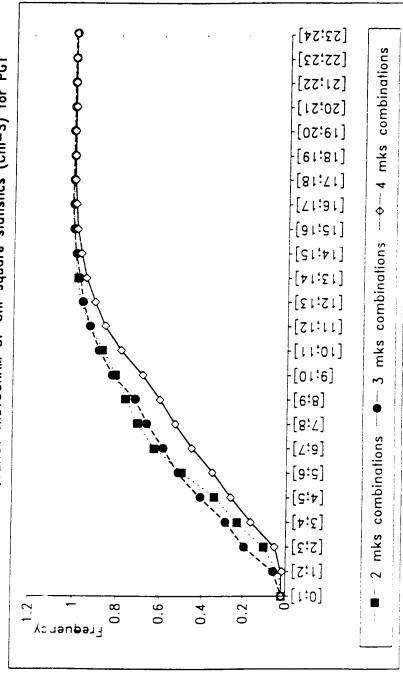
ND Not Done

113.21

Comparison of Pvalue between nb of mks for haplotype (19 mks of PG1)

ſ		1
	# of mks combinations	3876
	# of 3 mks combinations	696
	# of 2 mks combinations	171
	# of markers	19
	GENE	PG1

CUMULATIVE FREQUENCY HISTOGRAM OF Chi-square statistics (Chi-S) for PG1



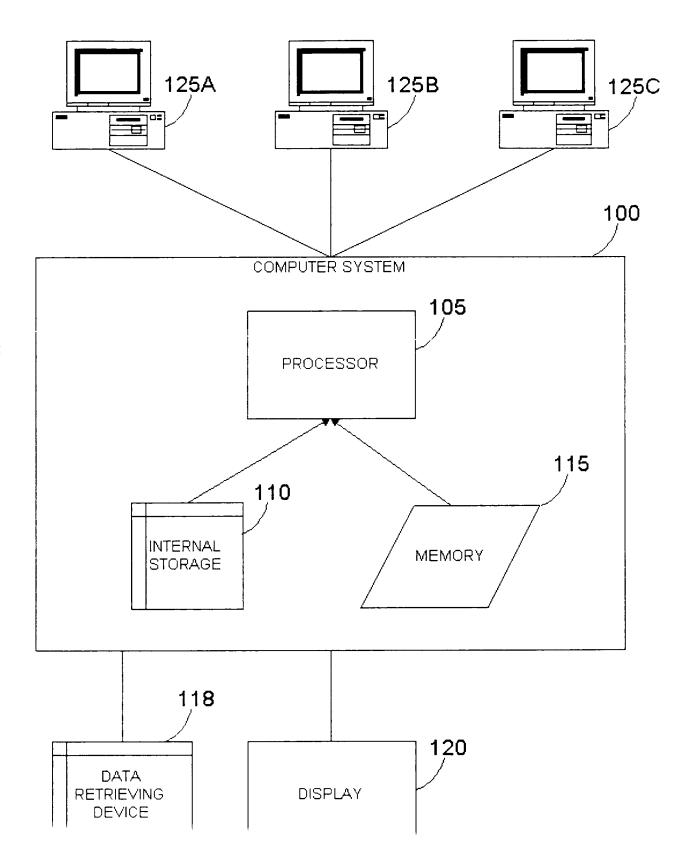
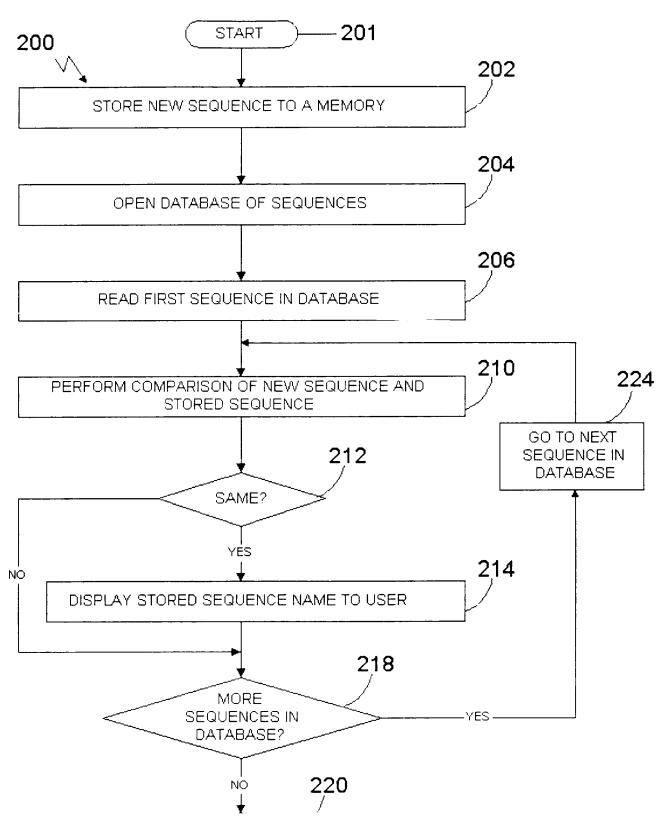


FIG. 22



=/G, _3

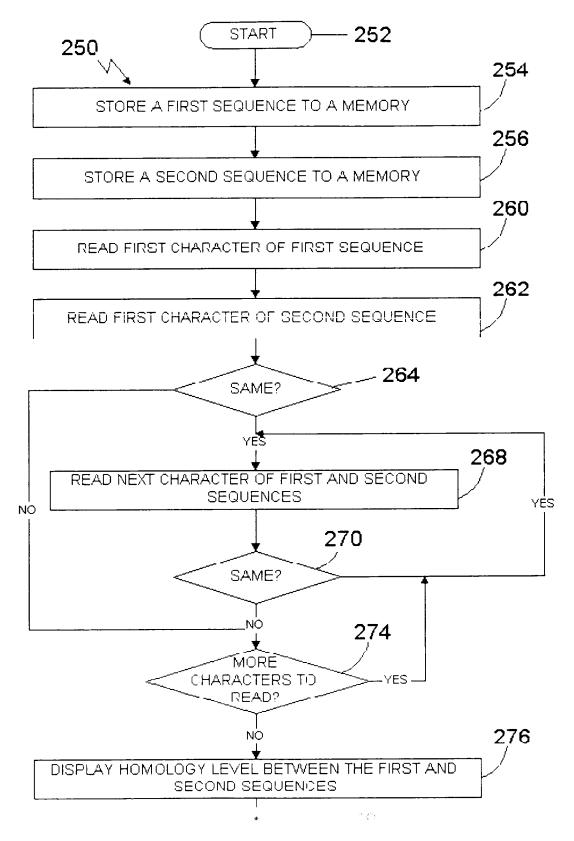


FIG. 24

